REMARKS

The Official Action dated February 9, 2006 and references cited therein have been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

Status of the Prosecution:

Claims 13, 29-43, 45-55, and 57-71 are pending in the application. All pending claims are rejected under 35 U.S.C. §112, first paragraph as allegedly not enabled, and under 35 U.S.C. §103(a) as an allegedly unpatentable over Hollingsworth *et al.* (1995) Genes Dev. 9:1728-39 ("Hollingsworth").

Current amendments to the specification and/or claims:

Claims 13, 29-30, 36-43, and 57-67 are canceled herein, without prejudice. Applicants submit that the remaining claims are in condition for allowance, as they satisfy all formal requirements and are directed to non-obvious subject matter. Support for Applicants' position is set forth below.

The claimed subject matter is fully enabled by the specification:

Claims 13, 29-43, 45-55, and 57-71 are rejected under 35 U.S.C. §112, first paragraph, as allegedly encompassing subject matter not enabled by the specification. The examiner avers that, although the specification is enabling for methods for identifying compounds that inhibit meiosis, it is not enabling for identifying compounds useful for contraception or preventing fertilization. According to the examiner, the specification fails to teach how the compounds are useful for contraception or preventing fertilization, and does

not provide examples of compounds or examples of their effectiveness. Applicants traverse the rejection.

Applicants disagree that independent claims 13, 30, 36, 37, directed to methods for identifying compounds useful as a contraceptive, and all claims that depend therefrom, are not enabled by the specification. Nevertheless, in an effort to facilitate prosecution, claims 13, 29-30, 36-43, and 57-67 are canceled herein, without prejudice. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation or divisional applications.

Applicants note that claims 31 and 32 are directed to methods to identify compounds useful for inhibiting meiosis. As the examiner has noted that such subject matter is fully enabled, applicants respectfully assert that such claims are not properly subject to the rejection, and withdrawal of the rejection is warranted.

The specification fully enables those of skill in the art to identify compounds that prevent fertilization. The description on page 7, lines 16-21, and page 14, lines 30-35 clearly outline parameters for the artisan to assess in screening for fertility, and indicates that the assays could be carried out *in vitro* (*e.g.*, on proteins, substrates, etc.) or *in vivo* (*e.g.*, in cells, transgenic animals, etc). Moreover, the working examples clearly show that $Msh5^{-/-}$ mice have disruption of spermatogenesis (page 18, line 29; Figure 2), germ cell attrition (page 19, line 3; Figure 3), failure to mate or undergo estrous cycles (page 19, lines 34-35), and have ovarian atrophy (page 19, line 35 bridging page 20 lines 1-13), among other things. Thus, the specification is replete with detailed examples of parameters that would enable the skilled artisan to practice the claimed methods to identify compounds that are useful for preventing fertilization.

Because the specification provides ample guidance to the skilled artisan as to how to practice the claimed methods, examples of specific compounds (and by extension, examples of their effectiveness) need not be disclosed. "The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." MPEP § 2164.02; *In re Borkowski,* 422 F.2d 904, 908 (CCPA 1970). Accordingly, reconsideration and withdrawal of the rejection is requested.

The claims are directed to subject matter that is not obvious from the cited reference:

Claims 13, 29-43, 45-55, and 57-71 are rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of the teachings of Hollingsworth. Hollingsworth is alleged to teach that MSH5 is a meiosis specific gene that is active to facilitate meiosis and meiotic chromosome synapsis (abstract) in bacteria, yeast, and humans (1729), and that mutant MSH5 or inhibited activity thereof results in decreased spore viability (1735-6). According to the examiner, Hollingsworth suggests that inhibited or reduced activity of MSH5 inhibits meiosis, inhibits chromosome synapsis, and decreases fertility, and that MSH5 is critical to these activities. It is further alleged that, despite Hollingsworth's lack of teaching of specific methods to identify compounds that inhibit meiosis, stimulate/inhibit chromosomal synapsis, prevent fertilization, or act as a contraceptive, such methods would be obvious. Applicants traverse the rejection.

Applicants note that the words "chromosome synapsis" and "facilitate meiosis" do not appear in the abstract as alleged by the examiner. Moreover, the abstract does not suggest a role for MSH5 in either of these functions. As such, the examiner's rationale is not supported.

Hollingsworth does not teach that MSH5 is a meiosis specific gene. The authors identified several new yeast alleles, including HOP1, RED1, and MEK1, which are specifically identified in the abstract as "meiosis-specific genes." The authors also identified a yeast gene designated MSH5. MSH5, however, was not listed among the other three alleles expressly designated as being meiosis specific. Moreover, it is clear that Hollingsworth was unsure if MSH5 had additional functions – as it is stated that MSH5 "*appears* to be restricted to meiosis," (page 1736) thus leaving open the possibility that MSH5 was not meiosis specific. Therefore, the examiner's view that Hollingsworth teaches that MSH5 is a meiosis specific gene is unsupported.

Hollingsworth does not teach or suggest that MSH5 is active to facilitate meiosis and meiotic chromosome synapsis in bacteria, yeast, or humans. With respect to bacteria and humans, the only mention of these two organisms takes place in the following context: "MutS homologs function in mismatch repair in a variety of different organisms, including

bacteria, yeast, and humans." (page 1729) The reference then goes on to state that "the MSH5 gene plays no role in DNA mismatch repair." Thus, the examiner's view that MSH5 can facilitate meiosis and synapsis in bacteria or humans is unsupported. If the examiner remains of the contrary view, applicants respectfully request supporting evidence pursuant to MPEP §2144.03.

With respect to yeast, there is no teaching, express or implied, that MSH5 facilitates meiosis or chromosome synapsis. The primary conclusions drawn from the experiments described in Hollingsworth were that MSH5 does not participate in DNA mismatch repair, and that MSH5 appears to facilitate reciprocal crossover among homologous chromosomes in yeast. There is no evidence anywhere in the reference that the authors understood MSH5 to facilitate meiosis or play any role in chromosome synapsis. Synapsis is the alignment of homologous chromosomes during early meiosis (see, *e.g.*, www.medterms.com). Crossover occurs subsequent to the alignment. There is no evidence or suggestion in the reference that MSH5 participates in chromosome alignment, or in any other process aside from reciprocal crossover, or that an effect on reciprocal crossover could affect the synapsis process. Thus, the examiner's view that MSH5 can facilitate meiosis and synapsis in yeast is unsupported. If the examiner remains of the contrary view, applicants respectfully request supporting evidence pursuant to MPEP §2144.03. Applicants concede no relationship of MSH5 to meiosis in yeast other than a possible role in reciprocal crossover exchange per the express teachings of Hollingsworth.

There is no teaching, express or implied, that MSH5 is "critical" to meiosis, the stimulation or inhibition of chromosome synapsis, fertilization, or contraception. With respect to meiosis, the examiner has apparently concluded from the observation that MSH5 mutant yeast demonstrate decreased spore viability, increased nondisjunction, and decreased reciprocal exchanges, that modulation of MSH5 inhibits meiosis. Applicants assert that such a conclusion is incorrect, and does not flow from the teachings of Hollingsworth. First, the fact that spores are produced at all means that meiosis is not inhibited. Second, the fact that spores that are produced exhibit decreased viability says nothing about the process of meiosis itself, but rather indicates only that the spore produced from meiosis is defective. Third, increased nondisjunction only indicates that the chromosomes fail to separate, but does not indicate that meiosis on the whole is inhibited or otherwise impaired. Fourth, decreased

reciprocal exchange indicates a defect in crossover, but does not indicate that meiosis on the whole is inhibited or otherwise impaired. As such, there is no evidence, express or implied, in Hollingsworth that the process of meiosis, or the rate at which meiosis proceeds in MSH5-mutant yeast is inhibited or impaired, or that the authors believed this to be the case. Thus, the examiner's view that affecting MSH5 inhibits meiosis in yeast is unsupported. If the examiner remains of the contrary view, applicants respectfully request supporting evidence pursuant to MPEP §2144.03.

As *Saccharomyces cerevisiae* is a budding yeast, there can be no suggestion from the teachings of Hollingsworth that yeast MSH5 is critical to fertilization or contraception. Thus, the examiner's view that MSH5 is critical to these activities is unsupported.

A *prima facie* case for obviousness has not been established. First, as acknowledged by the examiner, Hollingsworth does not teach or suggest all of the limitations of the claimed invention. The invention relates to methods to identify compounds useful as a contraceptive, to inhibit meiosis in a cell, to prevent fertilization in a subject, to stimulate chromosome synapsis in a cell, and to inhibit chromosome synapsis in a cell. Hollingsworth does not teach or suggest any such methods.

Second, there is no suggestion or motivation, either from the reference itself or from knowledge generally available in the art, to modify the teachings of Hollingsworth to arrive at the claimed invention. As detailed above, Hollingsworth provides no express or implied connection between MSH5 and the rate of meiosis, whether or not meiosis occurs, chromosome synapsis, fertilization, or contraception. There is no teaching or suggestion that modulation of MSH5 would have any inhibitory effects on meiosis, would have any effect on fertility, would have any effect on chromosome synapsis, or would have any utility as a contraceptive. Given the limited teachings of Hollingsworth, the skilled artisan would not reason the claimed methods. Thus, the apparent motivation to modify can come only from the teachings of the present disclosure, which is improper. Thus, a *prima facie* case for obviousness has not been established, and withdrawal of the rejection is warranted.

Conclusion:

In view of the amendments submitted herewith and the foregoing remarks, Applicants respectfully assert that all claims presently pending are in condition for allowance. Favorable reconsideration and a Notice of Allowance are earnestly requested.

Respectfully submitted,

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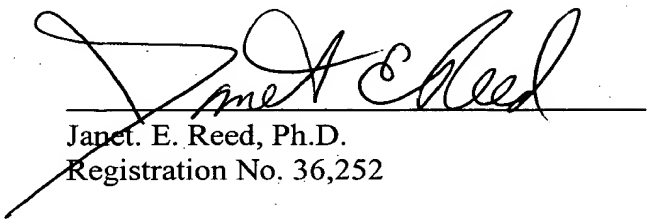

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